Amendments to the Specification:

Please replace the paragraph beginning at page 29, line 12 with the following corrected paragraph:

The extracellular ligand binding domain is defined as the portion of a receptor that, in its native conformation in the cell membrane, is oriented extracellularly where it can contact with its cognate ligand. The extracellular ligand binding domain does not include the hydrophobic amino acids associated with the receptor's transmembrane domain or any amino acids associated with the receptor's intracellular domain. Generally, the intracellular or cytoplasmic domain of a receptor is usually composed of positively charged or polar amino acids (i.e. lysine, arginine, histidine, glutamic acid, aspartic acid). The preceding 15-30, predominantly hydrophobic or apolar amino acids (i.e. leucine, valine, isoleucine, and phenylalanine) comprise the transmembrane domain. The extracellular domain comprises the amino acids that precede the hydrophobic transmembrane stretch of amino acids. Usually the transmembrane domain is flanked by positively charged or polar amino acids such as lysine or arginine. von Heijne has published detailed rules that are commonly referred to by skilled artisans when determining which amino acids of a given receptor belong to the extracellular, transmembrane, or intracellular domains (See von Heijne, 1995, BioEssays 17:25-30). Alternatively, websites on the Internet, ~~such as http://ulrec3.unil.ch/software/TMPRED_form.html.~~ have become available to provide protein chemists with information about making predictions about protein domains.

Please amend the paragraph beginning on page 16 at line 16 with the following rewritten paragraph:

Figure 2. Binding of unmodified Flt1(1-3)-Fc and acetylated Flt1(1-3)-Fc proteins to ~~Matrigel®~~ MATRIGEL™ (a trademark of Becton, Dickinson & Co. relating to solubilized basement membrane preparations) coated plates. Unmodified Flt1(1-3)-Fc proteins binds extensive to extracellular matrix components in ~~Matrigel®~~ MATRIGEL™, whereas acetylated Flt1(1-3)-Fc does not bind.

Please amend the paragraph beginning on page 16, line 21 to page 17, line 4, with the following rewritten paragraph:

Figure 3. Binding of unmodified Flt1(1-3)-Fc, acetylated Flt1(1-3)-Fc, and pegylated Flt1(1-3)-Fc in a ~~Biacore~~ BIACORE™ (a trademark of Biacore AB relating to systems for protein interaction analysis)-based assay. Acetylated (columns 13-16), pegylated (columns 17-20), and heparin-treated Flt1(1-3)-Fc (columns 21-24) are each able to completely compete with the Biacore chip-bound Flt1(1-3)-Fc for VEGF binding as compared to control (columns 1-4) and irrelevant protein (columns 5-8). Unmodified Flt1(1-3)-Fc (columns 5-6) appears to only partially compete with Biacore chip-bound

Flt1(1-3)-Fc for VEGF binding. However, washing the bound samples with 0.5M NaCl (columns 7-8) results in a binding profile similar to the modified forms of Flt1(1-3)-Fc, indicating that the unmodified protein is exhibiting non-specific binding to the chip that can be eliminated by the salt wash.

Please amend the paragraph beginning on page 24 at line 20 with the following rewritten paragraph:

Figure 32. Size Exclusion Chromatography (SEC) under dissociative conditions. To separate the components of the receptor-ligand complex and to determine their molar ratio, 50µl of dissociated complex was loaded onto a ~~Superose 12 PC~~ SUPEROSE 12 PC™ (a trademark of Amerisham Pharmacia Biotech AG relating to sensitive and high resolving gel filtration separations of proteins, peptides, polynucleotides and other biomolecules in the micropreparative scale) 3.2/30 equilibrated in 6M GuHCl and eluted. Peak #1 represents Flt1D2Flk1D3.FcΔC1(a) and peak #2 represents VEGF165.

Please amend the paragraph beginning on page 38 at line 24 with the following rewritten paragraph:

All chemicals were obtained from J.T. Baker, Phillipsburg, NJ with the exception of PBS, which was obtained as a 10X concentrate from Life Technologies, Gaithersburg, MD. Protein A Fast Flow and ~~Superdex 200~~ SUPERDEX 200™ (a trademark of Amerisham Pharmacia Biosciences relating to a prepacked column for high performance of gel filtration of protein, DNA fragments and other biomolecules) preparation grade resins were obtained from Pharmacia, Piscataway, NJ. Equipment and membranes for protein concentration were obtained from Millipore, Bedford, MA.

Please amend the paragraph beginning on page 51 at line 14 with the following rewritten paragraph:

A more detailed analysis of the Flt1 amino acid sequence reveals that there is a cluster, namely, amino acid residues 272-281 (KNKRASVRR) of Figure 10A-10D, in which 6 out of 10 amino acid residues are basic. This sequence is located in Flt1 Ig domain 3 of the receptor (see Figure 11), which is not itself essential for binding of VEGF ligand, but which confers a higher affinity binding to ligand. An alignment of the sequence of Ig domain 3 with that of Ig domain 2 reveals that in this region, there is very poor alignment between the two Ig domains, and that there are about 10 additional amino acids in Ig domain 3. An analysis of the hydrophilicity profiles (~~MacVector~~ MACVECTOR™, a trademark of Accelrys relating to computer software) of these two domains clearly indicates the presence of a hydrophilic region in the protein (Figure 12A-12B). These observations raised the possibility that the actual three dimensional conformation of Flt1 Ig domain 3 allowed for some type of protrusion that is not in Flt1 Ig domain 2. To test this hypothesis, the 10 additional amino acids were deleted and the resulting protein was tested to see whether the deletion

would affect the pharmacokinetics favorably without seriously compromising the affinity of the receptor for VEGF. This DNA construct, which was constructed using standard molecular biology techniques (see e.g., Molecular Cloning, A Laboratory Manual (Sambrook, et al., Cold Spring Harbor Laboratory), Current Protocols in Molecular Biology (Eds. Ausubel, et al., Greene Publ. Assoc., Wiley-Interscience, NY) in the mammalian expression vector pMT21 (Genetics Institute, Inc., Cambridge, MA), is referred to as Mut1: Flt1(1-$3_{\Delta B}$)-Fc. The Mut1: Flt1(1-$3_{\Delta B}$)-Fc construct was derived from Flt1(1-3)-Fc by deletion of nucleotides 814-843 (set forth in Figure 10A-10D), which deletes the highly basic 10-amino acid residue sequence Lys-Asn-Lys-Arg-Ala-Ser-Val-Arg-Arg-Arg from Flt1 Ig domain 3.

Please amend the paragraph beginning on page 65 at line 23 with the following rewritten paragraph:

Example 19: Transient expression of pFlt1D2.Flk1D3.FcΔC1(a) in CHO-K1 (E1A) cells

A large scale (2L) culture of E. coli DH10B cells carrying the pFlt1D2.Flk1D3.FcΔC1(a) plasmid described *supra* in Example 17(a) was grown overnight in Terrific Broth (TB) plus 100µg/ml ampicillin. The next day, the plasmid DNA was extracted using a QIAgen ~~Endofree~~ ENDOFREE™, a trademark of Quigen relating to a Megaprep kit following the manufacturer's protocol. The concentration of the purified plasmid DNA was determined by standard techniques using a UV spectrophotometer and fluorometer. The plasmid DNA was verified by standard restriction enzyme digestion of aliquots using the restriction enzymes EcoRI plus NotI and AseI. All restriction enzyme digest fragments corresponded to the predicted sizes when analyzed on a 1% agarose gel.

Please amend the paragraph beginning on page 66 at line 10 with the following rewritten paragraph:

Forty 15 cm petri plates were seeded with CHO-K1/E1A cells at a density of 4 x 106 cells/plate. Plating media was Gibco Ham's F-12 supplemented with 10% ~~Hyclone~~ HYCLONE™ (a trademark of Hyclone Laboratories relating to chemical products for scientific research, medical research, and the production of pharmaceuticals) Fetal Bovine Serum (FBS), 100U penicillin/100U streptomycin and glutamine (2mM). The following day each plate of cells was transfected with 6 µg of the pFlt1D2.Flk1D3.FcΔC1(a) plasmid DNA using Gibco Optimem and Gibco Lipofectamine in 12 ml volume, following the manufacturer's protocol. Four hours after adding the transfection mix to the cells, 12 ml/plate of Optimem supplemented with 10% FBS was added. Plates were incubated at 37°C in a 5% CO_2 incubator overnight. The following day the media was removed from each plate and 25 ml expression media (Gibco CHO-S-SFM II supplemented with glutamine (2mM) and 1mM sodium butyrate) was added. The plates were incubated at 37°C for 3 days. After 3 days of incubation, the media was aspirated from each plate and centrifuged at 400 rpm in a swinging

bucket rotor to pellet cells. The supernatant was decanted into sterile 1L bottles and purification of the expressed protein was performed as described *infra*.

Please amend the paragraph beginning on page 69 at line 21 with the following rewritten paragraph:

Example 22: Harvest and Purification of Modified Flt1 Receptors

(a) Harvest and Purification of Flt1D2.Flk1D3.FcΔC1(a)

The product protein was aseptically harvested from the bioreactor while retaining cells using Millipore Prostak tangential-flow filtration modules and a low-shear mechanical pump (Fristam). Fresh medium was added to the bioreactor to replace that removed during the harvest filtration. Approximately 40L of harvest filtrate was then loaded onto a 400 mL column containing Protein A ~~Sepharose~~ SEPHAROSE™ (a trademark of Amersham Biosciences relating to signal transduction and cell trafficking) resin ~~(Amersham Pharmacia)~~. After loading the resin was washed with buffer containing 10 mM sodium phosphate, 500 mM sodium chloride, pH 7.2 to remove any unbound contaminating proteins. Flt1D2.Flk1D3.FcΔC1(a) protein was eluted with a pH 3.0 citrate buffer. The eluted protein was neutralized by addition of Tris base and frozen at -20°C.